

Applicant: Cy A. Stein  
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Listing of Claims

1-8. (Canceled)

9. (Currently Amended) A composition of matter comprising an antisense oligonucleotide comprising consecutive nucleotides, the nucleotide sequence of which is set forth in one of SEQ ID NOS:1 and 3-13, wherein one or more sugar of the oligonucleotide contain an -OMe group at its 2' position and wherein the oligonucleotide is complementary to a bcl-xL-encoding mRNA and inhibits translation thereof.

10-25. (Canceled)

26. (Currently Amended) A method of promoting the regression of vascular lesions, comprising introducing into a vascular cell an amount of a composition of matter comprising an antisense oligonucleotide comprising consecutive nucleotides, the nucleotide sequence of which is set forth in one of SEQ ID NOS:1 and 3-13, effective to reduce the levels of bcl-xL protein produced, thereby promoting the regression of vascular lesions, wherein one or more sugar of the oligonucleotide contain an -OMe group at its 2' position and wherein the oligonucleotide is complementary to a bcl-xL-encoding mRNA and inhibits translation thereof.

27. (Previously Presented) The method of claim 26, wherein the introducing comprises using a lipid as a delivery agent.

28. (Previously Presented) The method of claim 26, wherein the introducing comprises using porphyrin as a delivery agent.

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29. (Previously Presented) The method of claim 26, wherein the effective amount is between 0.1  $\mu$ M and 4  $\mu$ M.
30. (Previously Presented) The method of claim 26, wherein the effective amount is between 0.4  $\mu$ M and 1  $\mu$ M.
31. (Canceled)
32. (Canceled)
33. (Canceled)
34. (Canceled)
35. (Canceled)
36. (Currently Amended) A composition of matter comprising an antisense oligonucleotide comprising consecutive nucleotides, the nucleotide sequence of which is set forth in one of SEQ ID NOS:1 and 3-13, wherein one or more sugar of the oligonucleotide is modified at its 2' position contain an -OMe group at its 2' position, wherein the oligonucleotide is complementary to a bcl-xL-encoding mRNA and inhibits translation thereof.
37. (Currently Amended) An antisense compound at least 10 nucleotides in length targeted to a nucleic acid molecule encoding a human bcl-x, wherein said antisense compound modulates the expression of human bcl-x, and wherein the nucleotide sequence of said antisense compound consists of SEQ ID NO:2 is an antisense oligonucleotide which comprises at least a 10 nucleobase portion of sequence B of Figure 1, and wherein one or more sugar of the oligonucleotide contain an -OMe group at its 2' position.

38. (Currently Amended) An antisense molecule at least 10 nucleotides in length targeted to a nucleic acid molecule encoding a human bcl-xl, wherein said antisense molecule downregulates the expression of human bcl-xl, and wherein said nucleotide sequence of said antisense compound consists of SEQ ID NO:2 ~~is an antisense oligonucleotide which comprises at least a 10 nucleobase portion of sequence B of Figure 1, and wherein one or more sugar of the oligonucleotide contain an -OMe group at its 2' position.~~

39. (Currently Amended) An antisense oligonucleotide or analog thereof comprising a sequence having 90% or greater identity to ~~sequence A,B,C,D,E,F,G,H,I,J,K,L, or M of Figure 1~~ SEQ ID NO:1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13, wherein the oligonucleotide is complementary to a nucleic acid molecule encoding a bcl-xl and wherein one or more sugar of the oligonucleotide contain an -OMe group at its 2' position.

40. (Currently Amended) An antisense oligonucleotide or analog thereof comprising a sequence having 85% or greater identity to ~~sequence A,B,C,D,E,F,G,H,I,J,K,L, or M of Figure 1~~ SEQ ID NO:1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13, wherein the oligonucleotide is complementary to a nucleic acid molecule encoding a bcl-xl and wherein one or more sugar of the oligonucleotide contain an -OMe group at its 2' position.

41. (Currently Amended) An antisense oligonucleotide or analog thereof comprising a sequence having 80% or greater

identity to sequence A,B,C,D,E,F,G,H,I,J,K,L, or M of Figure 1 SEQ ID NO:1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13, wherein the oligonucleotide is complementary to a nucleic acid molecule encoding a bcl-xl and wherein one or more sugar of the oligonucleotide contain an -OMe group at its 2' position.

42. (Currently Amended) An antisense oligonucleotide or analog thereof comprising a sequence having 75% or greater identity to sequence A,B,C,D,E,F,G,H,I,J,K,L, or M of Figure 1 SEQ ID NO:1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13, wherein the oligonucleotide is complementary to a nucleic acid molecule encoding a bcl-xl and wherein one or more sugar of the oligonucleotide contain an -OMe group at its 2' position.
43. (Currently Amended) An antisense oligonucleotide or analog thereof comprising a sequence having 70% or greater identity to sequence A,B,C,D,E,F,G,H,I,J,K,L, or M of Figure 1 SEQ ID NO:1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13, wherein the oligonucleotide is complementary to a nucleic acid molecule encoding a bcl-xl and wherein one or more sugar of the oligonucleotide contain an -OMe group at its 2' position.
44. (Previously Presented) The antisense oligonucleotide of claim 37,38,39,40,41, 42 or 43 which comprises at least one modified internucleoside linkage.
45. (Previously Presented) The antisense oligonucleotide of claim 44, wherein the modified internucleoside linkage is phosphorothioate linkage.
46. (Previously Presented) The antisense oligonucleotide of

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claim 44, wherein the modified internucleoside linkage is a morpholino linkage.

47. (Previously Presented) The antisense oligonucleotide of claim 37,38,39,40,41, 42 or 43, which comprises at least one modified sugar moiety.
48. (Previously Presented) The antisense oligonucleotide of claim 37,38,39,40,41, 42 or 43, which comprises at least one modified nucleobase.
49. (Previously Presented) The antisense oligonucleotide of claim 48, wherein the modified nucleobase is a 5-methylcytosine.
50. (Previously Presented) The antisense oligonucleotide of claim 37,38,39,40,41, 42 or 43, which is a chimeric oligonucleotide.
51. (Currently Amended) An antisense oligonucleotide comprising nucleotide sequence ~~G of Figure 1~~ SEQ ID NO:7.
52. (Currently Amended) An antisense oligonucleotide comprising at least 10 contiguous nucleotides of nucleotide sequence ~~G of Figure 1~~ SEQ ID NO:7.
53. (Canceled).
54. (Currently Amended) The antisense oligonucleotide of claim 37,38,39,40,41,42 or 43 53, wherein substantially all the oligonucleotide's sugars contain an -Ome group at their 2' position.

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55. (Previously Presented) A method of inhibiting the expression of bcl-xL in human cells or tissues in vitro comprising contacting said cells or tissues with the antisense oligonucleotide of claim 37,38,39,40,41, 42 or 43 so that the expression of bcl-xL is inhibited.
56. (Previously Presented) A method of treating cancer, comprising administering to a patient in need of such treatment the antisense oligonucleotide of claim 37,38,39,40,41, 42 or 43.
57. (Previously Presented) The method of claim 56, further comprising administering chemotherapy to the patient.
58. (Previously Presented) A pharmaceutical composition comprising an effective amount of the antisense oligonucleotide or analog thereof of claim 37,38,39,40,41, 42 or 43 and a pharmaceutically acceptable carrier.
59. (Previously Presented) A method of treating cancer, comprising administering to a patient in need of such treatment the pharmaceutical composition of claim 58.
60. (Previously Presented) The method of claim 59, further comprising administering chemotherapy to the patient.
61. (Previously Presented) The pharmaceutical composition of claim 58, further comprising a colloidal dispersion system.
62. (Previously Presented) An antisense compound at least 10 nucleotides in length targeted to a nucleic acid molecule encoding a human bcl-x, wherein said antisense compound modulates the expression of human bcl-x, and wherein said antisense compound is an antisense oligonucleotide which

comprises at least a 10 nucleobase portion of sequence C,D,E,F,G,I and M of Figure 1.

63. (Previously Presented) An antisense oligonucleotide consisting of consecutive nucleotides, the nucleotide sequence of which is set forth in SEQ ID NO:2, wherein one or more sugar of the oligonucleotide contain an -OMe group at its 2' position.
64. (Currently Amended) A method of promoting the regression of vascular lesions, comprising introducing into a vascular cell an amount of an antisense oligonucleotide consisting of consecutive nucleotides, the nucleotide sequence of which is set forth in SEQ ID NO:2, effective to reduce the levels of bcl-xL protein produced by the vascular cell, thereby promoting the regression of vascular lesions, wherein one or more sugar of the oligonucleotide contain an -OMe group at its 2' position and wherein the oligonucleotide is complementary to a nucleic acid molecule encoding a bcl-xL.
65. (Previously Presented) An antisense oligonucleotide consisting of consecutive nucleotides, the nucleotide sequence of which is set forth in SEQ ID NO:2, wherein one or more sugar of the oligonucleotide is modified at its 2' position.
66. (New) The composition of matter of claim 1, wherein the oligonucleotide is encapsulated in a liposome or nanoparticle.
67. (New) A method of promoting the regression of vascular lesions, comprising introducing into a vascular cell an

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effective amount of the composition of matter of claim 1, effective to reduce the levels of bcl-xL protein produced, thereby promoting the regression of vascular lesions, wherein one or more sugar of the oligonucleotide contain an -OMe group at its 2' position and wherein the oligonucleotide is complementary to a nucleic acid molecule encoding a bcl-xL.

68. (New) The composition of matter of claim 1, wherein the oligonucleotide is linked to an intercalating agent, a cross-linker, an endonuclease, an alkylating agent, a coordination complex, or a combination thereof.
69. (New) The composition of matter of claim 1, wherein the oligonucleotide is modified to reduce its ionic charge or increase its hydrophobicity.
70. (New) The composition of matter of claim 1, wherein the oligonucleotide comprises one or more short chain alkyl structures that replace some of the oligonucleotide's phosphodiester bonds.
71. (New) The composition of matter of claim 1, wherein the oligonucleotide is linked to one or more cholesteryl moieties.
72. (New) The composition of matter of claim 1, wherein the oligonucleotide comprises one or more bases with a C-5 propynyl pyrimidine modification.